

Abstract

The growth hormone supergene family comprises greater than 20 structurally related cytokines and growth factors. A general method is provided for creating site-specific, biologically active conjugates of these proteins. The method involves adding
5 cysteine residues to non-essential regions of the proteins or substituting cysteine residues for non-essential amino acids in the proteins using site-directed mutagenesis and then covalently coupling a cysteine-reactive polymer or other type of cysteine-reactive moiety to the proteins via the added cysteine residue. Disclosed herein are preferred sites for adding cysteine residues or introducing cysteine substitutions into
10 the proteins, and the proteins and protein derivatives produced thereby. Also disclosed are therapeutic methods for using the cysteine variants of the invention.